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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,440	02/18/2004	Linda N. Liu	AO-MAXC:002US	3491

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,440	LIU ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *16-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/18/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/10/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-15 and 34-37, in the reply dated 1/13/2005 is acknowledged.

Claims 16-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/13/2005.

Priority

This application, filed 2/18/2004, claims benefit of application 60/448,670, filed 2/18/2003. The instant invention is granted a priority date of 2/18/2003.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3, 5, 6, 8-15, and 34-37 are rejected under 35 U.S.C. 102(a) as being anticipated by Duke et al (WO 02/39951, cited by applicants, published 6/23/2002). The claims are drawn to a method of loading an antigen-presenting cell (APC) with one or more antigens comprising: mixing the APC and the antigen composition, which may comprise one or more antigens of a hyperproliferative cell, a microorganism-infected cell, or a microorganism; and electroporating the mixture such that the antigen(s) are loaded into the APC. The APC may be a dendritic cell

and the microorganism may be a virus, bacterium, fungus, or protozoan. The antigens may comprise a lysate, be tumor-associated (TAA) or tumor-restricted (TRA) antigens, and the TAA may be recombinant. The lysate may be a tumor cell lysate, which may be from autologous or allogeneic tumors, or a cancer cell lysate. The cancer cell lysate may be from any of the cancers listed in claim 15. Also claimed (claims 34-37) is a composition comprising an APC loaded with one or more antigens. Claims 34-37 recite a product (loaded APC) by process (flow electroporation). Product-by-process claims are not limited to the manipulations of the recited steps. See MPEP 2113. As such, the invention of claims 34-37 is considered to be a composition comprising an APC loaded with one or more antigens from a hyperproliferative cell, a microorganism-infected cell, or a microorganism. The APC may be a dendritic cell and the composition may be a pharmaceutical composition suitable for delivery to a subject, which may be a human subject.

Duke et al disclose a method to produce a dendritic cell (and a cell so produced) loaded with a yeast particle (a microorganism and a fungus) and an antigen. The loading may be accomplished by electroporation (see paragraph bridging pages 3-4). The antigen may be from a lysate, which may be prepared with detergent (SDS, page 31, lines 19-21), expressed from a recombinant nucleic acid molecule, and may be from tumor cells or microorganisms (page 12, first full paragraph). The antigen may be a tumor cell lysate, which may be autologous or allogeneic, or from a cancer cell, which may be breast cancer, one of the cancers listed in claim 15 (see page 13 second full paragraph to page 14 first full paragraph). Also disclosed are antigens listed by applicants as TAAs (page 14 of the instant specification), such as MAGE and CEA (page 14, lines 20-21). Tumor cells and tumor cell lysates are considered, absent evidence

to the contrary, to comprise TRAs, defined by applicants to be antigens upregulated or expressed only in tumor cells (page 14 of the instant specification). The loaded dendritic cell may be used as a therapeutic composition delivered with a pharmaceutically acceptable excipient (page 4, lines 14-22) to a human (page 27, lines 24-26).

Claims 1-2, 8, 10, 34 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Scott-Taylor et al (cited by applicants, 2000). The claims are as described above. Although Scott-Taylor et al use the term "electrofusion" to describe the preparation of cells, this is considered to by synonymous with "electroporation" as defined by applicants on page 22 of the specification: "..application of an electrical current or electrical field to a cell to facilitate entry of...an antigen composition into the cell.".

Scott-Taylor et al disclose the fusion of MCF-7 and LNCaP tumor cells with dendritic cells by application of an electric current from a Bio-Rad Gene Pulser electroporation apparatus (see the abstract; page 273, second column, first full paragraph; and Fig. 4). Because the antigens of the tumor cells are now within the dendritic cells, this is considered loading. The tumor cells are considered to comprise both TAAs and TRAs for the reasons cited above.

Claims 1-2, 8, 10 and 34-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Kugler et al (Nat. Medicine, 2000). The claims are as described above. Kugler et al describe the electrofusion of dendritic and renal cell tumor cells (pages 335-336, paragraphs entitled "Tumor and dendritic cells" and "Generation of hybrid cell vaccine"), and the composition was injected subcutaneously into seventeen human patients and was well tolerated (see page 335, paragraph

entitled "Treatment" first full paragraph page 333, first column, and paragraph bridging the first and second columns, page 333). Therefore, it was suitable for delivery to human subjects. The tumor cells are considered to comprise both TAAs and TRAs for the reasons cited above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-8, 10, 11, 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asavaroengchai et al (PNAS, January, 2002) in view of Kim et al (FASEB J., Abstract, page A664, March, 2002) or Chen et al (cited by applicants, 1993), and in further view of Spetz et al. (J. Immunol., 2002).

The claims are described above, except the antigen composition may comprise a

microorganism-infected cell infected with virus, bacterium, fungus, or protozoan, and the lysate may be prepared by detergent or non-detergent treatment. The non-detergent treatment may be any of those listed in claim 7. Asavaroengchai et al disclose a method of loading murine dendritic cells with tumor cell lysates by pulsing (incubating) the dendritic cells with the lysates. The lysates were generated by freeze-thaw cycles, one of the methods of claim 7 (See abstract and paragraph bridging the first and second columns, page 932). The tumor cell lines were derived from mammary (MT-901) or lymphatic cancers (A20), both of which are listed in claim 15, and are considered to comprise TAAs and TRAs for reasons cited above (paragraph bridging pages 931-932). The tumors are considered allogeneic because they were derived from genetically different animals of the same species.

Asavaroengchai et al do not explicitly teach the use of electroporation to load dendritic cells or the use of microorganism-infected cells as an antigen source.

Kim et al teach the loading of dendritic cells by electroporation, and that the reason for this was to compare electroporation with pulsing as methods for loading dendritic cells with antigen. The reference teaches that dendritic cells loaded by electroporation presented more MHC-I determinants and induced a more efficacious immune response than cells loaded by pulsing. The authors conclude electroporation is a useful way to enhance MHC-I mediated antitumor immunity.

Chen et al teach the loading of APCs with the antigen ovalbumin by electroporation, and that the reason for this was to direct antigen to the cytoplasm and thus the MHC-I pathway (see abstract, Introduction on pages 49-50, the first full paragraph, second column, page 50, and Fig. 2, page 52). The reference teaches that loading of APCs by electroporation is efficient and easy

relative to other methods current of the time (osmotic loading, linkage to lipophiles, etc, see page 50, first column).

Spetz et al teach mouse splenocytes infected with a HIV-1/MuLV hybrid retrovirus, produced to study the immune response to HIV-1 (see abstract and Materials and Methods "Production of syngeneic apoptotic HIV-1/MuLV-infected cells", column 1, page 5772). The reference teaches that mouse splenocytes infected with a HIV-1/MuLV hybrid retrovirus are a source of antigen(s) for immunization.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Asavaroengchai et al to load dendritic cells (or APC in general) by electroporation and to use micro-organism infected cells as an antigen source because it was known in the art at the time of filing that electroporation could load antigen into APC and that retrovirus-infected cells are an effective source of antigen. One would have been motivated to do so in order to receive the expected benefits of improved loading efficiency taught by Chen et al along with the improved MHC-I presentation and immunogenicity taught by Kim et al. Further motivation would be to develop an effect HIV-1 vaccine using the retrovirus-infected cells of Spetz et al. Given the teachings of the cited art, the state of the art at the time of applicants invention, and absent evidence to the contrary, there would have been a reasonable expectation of success in utilizing the electroporation taught by Kim et al and Chen et al in the methods taught by Asavaroengchai et al for antigen loading of APC, one such antigen being retrovirus-infected cells.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1636

PRIMARY EXAMINER